CONTROLLED RELEASE POTASSIUM CHLORIDE

CROSS REFERENCE TO RELATED APPLICATIONS

This application is a continuation-in-part of Ser. No. 702,714, filed Feb. 19, 1985 now abandoned.

FIELD OF THE INVENTION

The present invention relates to a controlled release potassium chloride tablet. More specifically, the present invention relates to a controlled release potassium chloride tablet comprised of polymer coated crystals of KCl which is orally administered to a patient requiring potassium supplementation which tablet provides for controlled release of the potassium chloride in the gastrointestinal tract and results in substantially less irritation to the gastric mucosa.

BACKGROUND OF THE INVENTION

It is well known that the administration of many diuretics increases the excretion of both sodium and potassium. The acute administration of such diuretics to a patient normally causes no problems. However, chronic administration of diuretics to the patient can result in the depletion of the potassium from the patient. For example, with patients having uncomplicated hypertension, the daily administration of diuretics produces a slight reduction in plasma potassium concentration. In edematous patients, the results are more variable. Some patients suffer from substantial depletion of potassium while others fail to show any evidence of depletion. There is a high incidence of severe potassium deficiency in patients treated simultaneously with diuretics and carbenoxolone which is an agent with mineralocorticoid activity.

As can be seen from the above discussion various treatments can result in potassium depletion, i.e., hypokalemia. Potassium depletion may be accompanied by a reduced tolerance to carbohydrates and a deficiency in glycogen deposition. Further, vasopressin-resistant polyuria is a prominent symptom. A deficit of potassium appears to increase the renal synthesis of prostaglandins, which in turn can decrease the permeability to water of the distal nephron and produce a diabetes insipidus-like syndrome.

When potassium is taken along with a normal diet it is slowly absorbed from the intestinal tract. Following distribution and uptake by the cells the kidneys excrete an appropriate amount to maintain a proper balance. As a consequence of the large volume of distribution and the rapid response of the kidney, the extracellular and intracellular concentrations of the ion are normally maintained within relatively narrow limits.

When potassium is administrated as a drug, the factors that can govern the rate and extent of its distribution are of major importance. It is not possible to increase the total body content of potassium significantly above normal. However, it is very easy to raise the extracellular concentration excessively. It is the concentration in the extracellular fluid that determines life-threatening toxicity. Therefore, even though the administered potassium is eventually destined either to be excreted or taken up by the cells, knowledge of the transient concentration achieved in the plasma must govern the use of potassium as a therapeutic agent.

It is well known that large doses of potassium chloride taken orally can cause GI irritation, purging, weakness and circulatory disturbances. Since potassium depletion can cause problems for the patient as indicated above a controlled release formulation of potassium chloride which would replenish potassium in a controlled manner without the undesirable side effects is badly needed. In an attempt to meet the need of providing dosage units which can be used as potassium supplements a number of different dosage forms have been developed. For example U.S. Pat. No. 4,352,791 discloses a composition comprised of potassium and a therapeutically acceptable salicylate salt of salicylic acid. The composition is used in potassium therapy and is useful in some respects but does not provide sufficient protection with respect to preventing gastric ulcers.

U.S. Pat. No. 4,340,582 discloses an enteric coated erythromycin tablet and a water-soluble nontoxic salt in the core. This core may be potassium chloride.

U.S. Pat. No. 4,259,323 discloses a potassium chloride emulsion which includes various ingredients in an attempt to mask the bad taste of the potassium chloride. However, dosing compliance utilizing an emulsion often causes problems in that the emulsion may settle and the patient may take different amounts of the emulsion and/or different amounts of the KCl in a given amount of emulsion.

U.S. Pat. No. 4,259,315 discloses a controlled release potassium dosage form used in treating potassium deficiency. The dosage form is comprised of gelatin capsules which contain a mixture comprised of controlled release forms of micro encapsulated potassium salt and a hydrophilic surfactant.

Sugar-coated tablets containing potassium chloride in a wax matrix (non-enteric-coated) are marketed as a slowly available potassium source. Physicians Desk Reference (1979), page 794, states "fewer bowel lesions are observed with wax-matrix tablets compared to enteric-coated potassium chloride products, but that there have been reports of upper gastrointestinal bleeding associated with the wax-matrix tablets. Use of these wax-coated products should be discontinued immediately and the possibility of bowel obstruction or perforation considered if severe vomiting, abdominal pain, distention or gastrointestinal bleeding occurs." (See U.S. Pat. No. 4,259,315).

A slow release pharmaceutical composition is disclosed within U.S. Pat. No. 4,235,870. The composition is comprised of a combination of higher aliphatic alcohols and hydrated hydroxyalkyl cellulose in a ratio of 2:1 to 4:1 parts by weight. The composition is intended to provide slow release of the therapeutically active compound during a predetermined period of time of from 5 to 10 hours after oral administration of the composition. However, this composition tends to remain intact and does not disintegrate, thus producing high concentrations of KCl.

Others have used surfactants to improve dissolution rate of drugs when powders agglomerate and teach the rate of dissolution is proportional to the reduction in surface tension of the gastric juice (Remington's Pharmaceutical Sciences, 15th Ed. (1973) p. 297). Others have used surfactants such as Polysorbate 20 as an ingredient interior to microcapsules during preparation of microcapsules and have discussed the adverse effect of such agents on the increased release rate of solids from the microcapsules (Luzzi et al. J. Pharm. Sci. 56(9), 1174–7 (1967). (See U.S. Pat. No. 4,259,315).